The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte GREGORY M. LANZA, SAMUEL A. WICKLINE, and CHRISTOPHER S. HALL

Appeal No. 2006-1031
Application No. 09/774,278

HEARD: May 9, 2006

Before ADAMS, MILLS, and GRIMES, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 3, 7, 8, 13, 17, 18, 21, 25, 26, 31, 35, and 68-77 which are pending in this application and on appeal.

Claim 1 is representative and reads as follows:

1. A method for comparing acoustic reflectivity of a target for ultrasound imaging at a lower and a higher temperature, the method comprising
(a) measuring reflectivity prior to raising the temperature of liquid nanoparticles bound to a target;
(b) raising the temperature of the liquid nanoparticles bound to said target sufficiently to produce a measurable enhancement in acoustic reflectivity of the target;
(c) measuring reflectivity after raising the temperature of the bound liquid nanoparticles; and
(d) determining the change in reflectivity of the bound liquid nanoparticles after raising the temperature compared to reflectivity prior to raising the temperature,

wherein said nanoparticles comprise at least one fluorocarbon,
said nanoparticles having been administered to said target in a non-gaseous emulsion.

The prior art reference cited by the examiner is:

Østensen et al. (Østensen)	6,375,931	Apr. 23, 2002

Grounds of Rejection

Claims 1, 3, 7, 8, 13, 17, 18, 21, 25, 26, 31, 35, and 68-77 stand rejected under 35 U.S.C. §102(e), as anticipated by Østensen.

Claims 1, 3, 7, 8, 13, 17, 18, 21, 25, 26, 31, 35, and 68-77 stand rejected under 35 U.S.C. §103(a), as obvious in view of Østensen.

We reverse these rejections.

DISCUSSION

Background

According to the specification, pages 3-4, it has been discovered that

> changing the temperature of nanoparticles which contain a nongaseous fluorocarbon liquid and which are bound to a target, produces a detectable change in acoustic reflectivity of the target. Non-targeted regions which are adjacent to the target, but are not bound by the nanoparticles, show little or no detectable change in acoustic reflectivity. As a result, the temperature-dependent change in acoustic reflectivity of site-targeted nanoparticles provides a sensitive measurement of ultrasound reflectivity and provides enhanced contrast imaging.

In addition, (specification, page 8)

> [a]ny fluorochemical liquid, i.e. a substance which is a liquid at or above body temperature (e.g. 37°C) at atmospheric pressure, can be used to prepare a fluorochemical emulsion of the present invention. However, for many purposes emulsions [of] fluorochemicals with longer extended

stability are preferred. In order to obtain such emulsions, fluorochemical liquids with boiling points above 50°C are preferred, and most preferred are fluorochemical liquids with boiling points above about 80°C. The guiding determinant should be that the oil, e.g. a fluorochemical, should be expected to remain in a liquid phase (less than 10% gas conversion) under the intended conditions of thermal induction and imaging.

According to the specification, page 8,

> [r]eference to the term 'nongaseous' or 'liquid' in the context of the nanoparticle emulsions of the present invention is intended to mean that less than 10% of the interior volume of the nanoparticles is in a gas phase per total volume of the nanoparticles (i.e. v/v), more preferably, no more than about 8% (v/v), more preferably no more than about 5% (v/v), and most preferably, no more than than 2% (v/v) or less. . . . The nanoparticle emulsions of the present invention are, preferably, lipid encapsulated. In a specific example, the lipid encapsulated particles may be constituted by a perfluorocarbon emulsion, the emulsion particles having an outer coating of a derivatized natural or synthetic phospholipid, a fatty acid, cholesterol, lipid, sphingomyelin, tocopherol, glucolipid, sterylamine, cardiolipin, a lipid with ether or ester linked fatty acids or a polymerized lipid.

102/103

Claims 1, 3, 7, 8, 13, 17, 18, 21, 25, 26, 31, 35, and 68-77 stand rejected under 35 U.S.C. §102(e), as anticipated by Østensen. Claims 1, 3, 7, 8, 13, 17, 18, 21, 25, 26, 31, 35, and 68-77 stand rejected under 35 U.S.C. §103(a), as obvious in view of Østensen.

According to the examiner (Answer, page 11)

> Ostensen discloses methods of performing ultrasound imaging comprising administering a perfluorocarbon emulsion comprising such perfluorocarbons as perfluoropentane, perfluorohexane, and even perfluorooctane to a specific region of a patient (see abstract, col 8, lines 1-60). . . .
>
> Ostensen teaches droplets that are smaller than 10 μm and thus meets the limitations of the instant nanoparticles, because the sizes of the instant nanoparticles as described in page 21, line[s]

> 7-10 of the specification encompass particles as large as 10 μm. (see Ostensen at [col. 7, lines 26-45;]col. 9, lines 34-38; col[s]. 35-37, and claim[s] 4-5, 16-18 wherein various perfluorocarbon emulsion mixtures are described).

The examiner further states at pages 4 and 5:

> Example[s] 5 and 10 of Ostensen describes Ostensen's process steps wherein a perfluorocarbon emulsion is administered to a mammal. Ostensen then teaches imaging of a specific site such as heart or kidney. Ostensen specifically expresses a steady rise in enhancement of the contrast images (see col. 39-40). As described by Ostensen, this steady rise of resonance intensity is attributed to an increase in microbubble size which is respectively caused by an increase in temperature of at least 5 Deg C of the perfluorocarbon liquid within the microbubbles of Ostensen. ...[P]erfluorobutane, perfluoropentane, perfluorohexane, and perfluoroheptanes are liquid at room temperature, and that microparticles containing such compounds increase in size when subject to ultrasound frequency. ... Ostensen discloses the use of targeted microbubbles comprising an RGD ligand that are specific for myocardium.

The examiner concludes that Østensen meets all the elements of the instant claims and therefore anticipates the claimed invention. Answer, page 5. The examiner argues that, "there is [sic, are] no teachings in the specification that excludes the formation of gas" in the liquid nanoparticles used in the claimed method. Answer, page 9.

Appellants respond, arguing (Brief, page 4), "Østensen does not disclose any methods at all that involve liquid nanoparticles. Østensen is concerned with the behavior of gas microbubbles." We agree, and therefore, do not find the examiner has established a prima facie case of anticipation or obviousness on the evidence before us.

According to the appellants' definition of "liquid nanoparticles" in the specification, the liquid nanoparticles of the invention may have no more than 10% gas. Appellants insist that claim 1 requires that in each step of the method the nanoparticles remain in liquid form. Brief, page 5. For example, appellants argue that "the statement by the Examiner ... [that] '[t]he instant step (b)-(d) does not exclude formation of a gas within the particles' is simply not true. Applicants have made clear throughout the prosecution that their particles are liquid, and do not contain gas." Id. In addition, appellants' Evidence Appendix, page 5, concludes that, in high intensity fields, the "backscatter from the liquid nanoparticles was due to simple linear backscatter from a liquid sphere and not from more esoteric processes such as phase conversion of the perfluorocarbon liquid inside the nanoparticles." Thus it would reasonably appear that appellants' liquid nanoparticles do not undergo a phase conversion to gas in high intensity ultrasonic fields.

In contrast, the contrast agent preparation of Østensen includes both an injectable medium having a gas dispersed therein and a composition comprising a diffusible component capable of diffusion in vivo into said dispersed gas so as to at least transiently increase the size thereof. Col. 2, lines 50-55. While Østensen recognizes that fluorocarbons and perfluorocarbons under standard conditions are liquid at normal body temperature (Column 13, lines 16-18), Østensen describes that "[a]ctivation of growth of the dispersed gas may be induced simply by release of excess pressure or by the heating to body temperature which will follow administration of the mixture, or it may if desired be brought about by the preheating the mixture immediately

before administration." Col. 14, lines 62-65. Østensen describes that, "it may be that the ultrasound pulses disrupt the encapsulating membrane and so enhance growth of the dispersed gas through inward diffusion of diffusible component in to the thus-exposed gas phase." Column 13, lines 4-8. Furthermore, Examples 2 and 4 of □stensen confirm that when the temperature is raised, there is a significant increase in the size of the microbubbles, i.e., the gas content of the microbubbles.

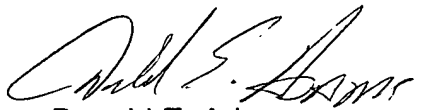
In view of the above, we do not find the examiner has established that the microbubbles of Østensen remain in liquid form throughout the performance of the imaging steps of the disclosed method, or that the microbubbles of Østensen do not contain more than 10% gas at any phase of the method in which the liquid microbubbles are used.

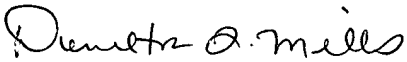
Nor do we find the examiner has established a prima facie case of obviousness on the evidence before us. With respect to the obviousness rejection, the examiner acknowledges that, "Østensen teaches the use of perfluoroctane, but fails to exemplify it. Ostensen also fails to administer his emulsion system to a human." Answer, page 7. The examiner concludes, "it would have been obvious to one of ordinary skill in the art at the time of [the] invention to modify Østensen's method and employ other art equivalent perfluorocarbon liquids such as perfluoroctane, in humans because the ordinary skill in the art would have had a reasonable expectation of success in observing optimal clinical results in humans as evident in dogs." Id.

In rejecting claims under 35 U.S.C. §103, the examiner bears the initial burden of presenting a prima facie case of obviousness. See In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). A prima facie case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art. In re Bell, 991 F.2d 781, 783, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993). An obviousness analysis requires that the prior art both suggest the claimed subject matter and reveal a reasonable expectation of success to one reasonably skilled in the art. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). We do not find the examiner has established, on the evidence before us, that the microbubbles of Østensen remain in liquid form throughout the performance of the imaging steps of the disclosed method, or that the microbubbles of Østensen do not contain more than 10% gas at any phase of the method in which the liquid microbubbles are used.

For this reason, the examiner has not established a prima facie case of anticipation or obviousness and the rejection of the claims for anticipation and for obviousness are reversed.

REVERSED



Donald E. Adams)
Administrative Patent Judge)
)
)

) BOARD OF PATENT
Demetra J. Mills)
Administrative Patent Judge) APPEALS AND
)

) INTERFERENCES
Eric Grimes)
Administrative Patent Judge)

Appeal No. 2006-1031
Application No. 09/774,278

Morrison & Foerster LLP
12531 High Bluff Drive
Suite 100
San Diego, CA 92130-2040

dem